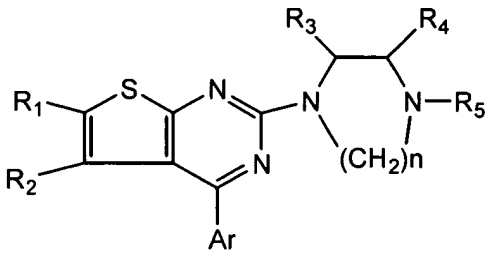
CLAIMS

What is claimed is:

1. A method of treating a functional bowel disorder in a subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound of Formula I:

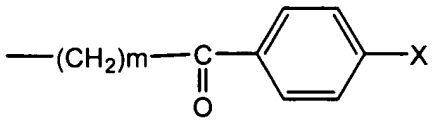


I

wherein, R_1 and R_2 independently represent hydrogen, halogen or a C_1-C_6 alkyl group; or R_1 and R_2 together with the carbon atom to which they are attached form a cycloalkylene group having 5 to 6 carbon atoms;

R_3 and R_4 independently represent hydrogen or a C_1-C_6 alkyl group;

R_5 is hydrogen, C_1-C_6 alkyl,



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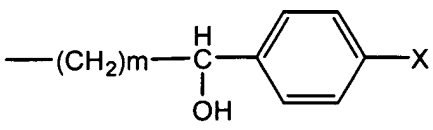


or -C(O)-NH-R_6

wherein m is an integer from about 1 to about 3, X is halogen and R_6 is a C_1-C_6 alkyl group; and

Ar is a substituted or unsubstituted phenyl, 2-thienyl or 3-thienyl group; and

n is 2 or 3; or a pharmaceutically acceptable salt thereof.

2. The method of Claim 1, wherein the functional bowel disorder is irritable bowel syndrome.

3. The method of Claim 2, wherein the irritable bowel syndrome is diarrhea predominant irritable bowel syndrome.

4. The method of Claim 2, wherein the irritable bowel syndrome is alternating constipation/diarrhea irritable bowel syndrome.

5. The method of Claim 2, wherein the irritable bowel syndrome is nonconstipated irritable bowel syndrome.

6. The method of Claim 1, wherein the subject is a human.

7. The method of Claim 1, wherein for the compound of Formula I, R_1 is a C_1-C_6 alkyl group and Ar is a substituted phenyl.

8. The method of Claim 7, wherein the substituted phenyl group is substituted with a halogen.

9. The method of Claim 1, wherein for the compound of Formula I, n is 2, R_1 is a C_1-C_6 alkyl group and Ar is a substituted phenyl.

10. The method of Claim 9, wherein the substituted phenyl group is substituted with a halogen and R_1 is a methyl group.

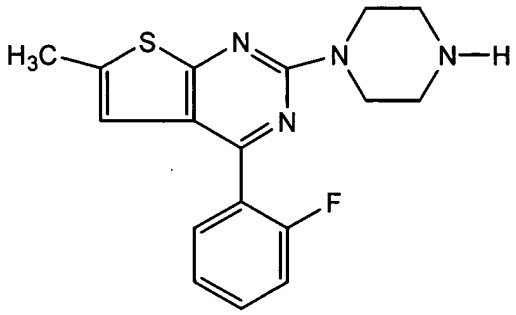
11. The method of Claim 1, wherein for the compound of Formula I, R_1 is a C_1-C_6 alkyl group or a halogen and Ar is an unsubstituted phenyl.

12. The method of Claim 11, wherein R_2 is hydrogen or a C_1-C_6 alkyl group.

13. The method of Claim 1, wherein for the compound of Formula I, n is 2, R_1 is a C_1-C_6 alkyl group and Ar is an unsubstituted phenyl.

14. The method of Claim 13, wherein R_2 is hydrogen or a C_1-C_6 alkyl group

15. A method of treating a functional bowel disorder in a subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound represented by Formula II:



II

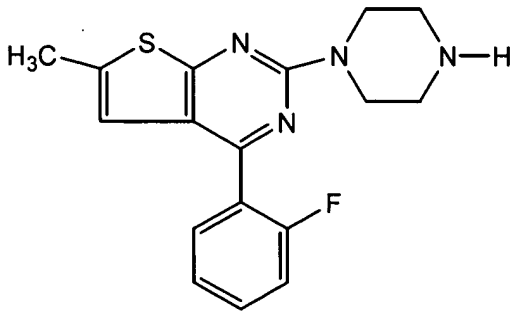
or a pharmaceutically acceptable salt thereof.

16. The method of Claim 15, wherein the functional bowel disorder is irritable bowel syndrome.

17. The method of Claim 16, wherein the irritable bowel syndrome is diarrhea predominant irritable bowel syndrome, alternating constipation/diarrhea irritable bowel syndrome or nonconstipated irritable bowel syndrome.

18. The method of Claim 15, wherein the subject is a human.

19. A method of treating diarrhea predominant irritable bowel syndrome in a subject in need thereof comprising administering to said subject a therapeutically effective amount of a compound represented by Formula II:



II

or a pharmaceutically acceptable salt thereof.

20. The method of Claim 19, wherein the subject is a human.

21. A method for treating a functional bowel disorder in a subject in need thereof comprising administering to said subject:

a) a first amount of a 5-HT_3 receptor antagonist; and

b) a second amount of a noradrenaline reuptake inhibitor

wherein the first and second amounts together comprise a therapeutically effective amount.

22. The method of Claim 21, wherein the functional bowel disorder is irritable bowel syndrome.

23. The method of Claim 22, wherein the irritable bowel syndrome is diarrhea predominant irritable bowel syndrome.

24. The method of Claim 22, wherein the irritable bowel syndrome is alternating constipation/diarrhea irritable bowel syndrome.

25. The method of Claim 22, wherein the irritable bowel syndrome is nonconstipated irritable bowel syndrome.

26. The method of Claim 21, wherein the subject is a human.

27. The method of Claim 21, wherein the 5-HT_3 receptor antagonist is selected from the group consisting of indisetron, YM-114 ((R)-2,3-dihydro-1-[(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl-)carbonyl]-1H-indole), granisetron, talipexole, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, N-3389, zacopride, cilansetron, E-3620 ([3(S)-endo]-4-amino-5-chloro-N-(8-methyl-8-azabicyclo[3.2.1-]oct-3-yl-2[(1-methyl-2-butynyl)oxy]benzamide), lintopride, KAE-393, itasetron, zatosetron, dolasetron, (±)-zacopride, (±)-renzapride, (-)-YM-060, DAU-6236, BIMU-8 and GK-128 [2-[2-methylimidazol-1-yl)methyl]-benzo[*f*]thiochromen-1-one monohydrochloride hemihydrate].

28. The method of Claim 27, wherein the 5-HT_3 receptor antagonist is selected from the group consisiting of indisetron, granisetron, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, cilansetron, itasetron, zatosetron, and dolasetron.

29. The method of Claim 21, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, buproprion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

30. The method of Claim 29, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

31. A method for treating a functional bowel disorder in a subject in need thereof comprising administering to said subject:

a) a therapeutically effective amount of a 5-HT_3 receptor antagonist; and

b) a therapeutically effective amount of a noradrenaline reuptake inhibitor.

32. The method of Claim 31, wherein the functional bowel disorder is irritable bowel syndrome.

33. The method of Claim 32, wherein the irritable bowel syndrome is diarrhea predominant irritable bowel syndrome.

34. The method of Claim 32, wherein the irritable bowel syndrome is alternating constipation/diarrhea irritable bowel syndrome.

35. The method of Claim 32, wherein the irritable bowel syndrome is nonconstipated irritable bowel syndrome.

36. The method of Claim 31, wherein the subject is a human.

37. The method of Claim 31, wherein the 5-HT_3 receptor antagonist is selected from the group consisting of indisetron, YM-114 ((R)-2,3-dihydro-1-[(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl-)carbonyl]-1H-indole), granisetron, talipexole, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, N-3389, zacopride, cilansetron, E-3620 ([3(S)-endo]-4-amino-5-chloro-N-(8-methyl-8-azabicyclo[3.2.1-]oct-3-yl-2[(1-methyl-2-butynyl)oxy]benzamide), lintopride, KAE-393, itasetron, zatosetron, dolasetron, (±)-zacopride, (±)-renzapride, (-)-YM-060, DAU-6236, BIMU-8 and GK-128 [2-[2-methylimidazol-1-yl)methyl]-benzo[*f*]thiochromen-1-one monohydrochloride hemihydrate].

38. The method of Claim 37, wherein the 5-HT_3 receptor antagonist is selected from the group consisiting of indisetron, granisetron, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, cilansetron, itasetron, zatosetron, and dolasetron.

39. The method of Claim 31, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, buproprion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

40. The method of Claim 39, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

41. A method of treating a functional bowel disorder in a subject in need thereof comprising administering to said subject a therapeutically effective amount of a noradrenaline reuptake inhibitor, wherein the noradrenaline reuptake inhibitor characterized by the substantial absence of anticholinergic effects.

42. The method of Claim 41, wherein the functional bowel disorder is irritable bowel syndrome.

43. The method of Claim 42, wherein the irritable bowel syndrome is diarrhea predominant irritable bowel syndrome.

44. The method of Claim 42, wherein the irritable bowel syndrome is alternating constipation/diarrhea irritable bowel syndrome.

45. The method of Claim 42, wherein the irritable bowel syndrome is nonconstipated irritable bowel syndrome.

46. The method of Claim 41, wherein the subject is a human.

47. The method of Claim 41, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, buproprion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

48. The method of Claim 47, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

49. A pharmaceutical composition comprising:

a) a first amount of a 5-HT_3 receptor antagonist; and

b) a second amount of a noradrenaline reuptake inhibitor.

50. The pharmaceutical composition of Claim 49, further comprising a pharmaceutically acceptable carrier.

51. The pharmaceutical composition of Claim 49, wherein the 5-HT_3 receptor antagonist is selected from the group consisting of indisetron, YM-114 ((R)-2,3-dihydro-1-[(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl-)carbonyl]-1H-indole), granisetron, talipexole, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, N-3389, zacopride, cilansetron, E-3620 ([3(S)-endo]-4-amino-5-chloro-N-(8-methyl-8-azabicyclo[3.2.1-]oct-3-yl-2[(1-methyl-2-butynyl)oxy]benzamide), lintopride, KAE-393, itasetron, zatosetron, dolasetron, (±)-zacopride, (±)-renzapride, (-)-YM-060, DAU-6236, BIMU-8 and GK-128 [2-[2-methylimidazol-1-yl)methyl]-benzo[*f*]thiochromen-1-one monohydrochloride hemihydrate].

52. The pharmaceutical composition of Claim 51, wherein the 5-HT_3 receptor antagonist is selected from the group consisting of indisetron, granisetron, azasetron, bemesetron, tropisetron, ramosetron, ondansetron, palonosetron, lerisetron, alosetron, cilansetron, itasetron, zatosetron, and dolasetron.

53. The pharmaceutical composition of Claim 49, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of venlafaxine, duloxetine, buproprion, milnacipran, reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

54. The pharmaceutical composition of Claim 53, wherein the noradrenaline reuptake inhibitor is selected from the group consisting of reboxetine, lefepramine, desipramine, nortriptyline, tomoxetine, maprotiline, oxaprotiline, levoprotiline, viloxazine and atomoxetine.

55. A method for processing a claim under a health insurance policy submitted by a claimant seeking reimbursement for costs associated with treatment of a functional bowel disorder, wherein said treatment comprises coadministering to a subject a first amount of a 5-HT_3 receptor antagonist and a second amount of a noradrenaline reuptake inhibitor, wherein the first and second amounts together comprise a therapeutically effective amount comprising:

a) reviewing said claim;

b) determining whether said treatment is reimbursable under said insurance policy; and

c) processing said claim to provide partial or complete reimbursement of said costs.

56. The method of Claim 55, wherein the functional bowel disorder is irritable bowel syndrome.

57. The method of Claim 56, wherein the irritable bowel syndrome is diarrhea predominant irritable bowel syndrome.

58. The method of Claim 56, wherein the irritable bowel syndrome is alternating constipation/diarrhea irritable bowel syndrome.

59. A method for processing a claim under a health insurance policy submitted by a claimant seeking reimbursement for costs associated with treatment of a functional bowel disorder, wherein said treatment comprises coadministering to a subject a therapeutically effective amount of a 5-HT_3 receptor antagonist and a therapeutically effective amount of a noradrenaline reuptake inhibitor comprising:

a) reviewing said claim;

b) determining whether said treatment is reimbursable under said insurance policy; and

c) processing said claim to provide partial or complete reimbursement of said costs.

60. The method of Claim 59, wherein the functional bowel disorder is irritable bowel syndrome.

61. The method of Claim 60, wherein the irritable bowel syndrome is diarrhea predominant irritable bowel syndrome.

62. The method of Claim 60, wherein the irritable bowel syndrome is alternating constipation/diarrhea irritable bowel syndrome.